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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,388	04/23/2002	Dolores Garcia Gravalos	211-213	6349

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EXAMINER

MCKENZIE, THOMAS C

ART UNIT PAPER NUMBER

1624

DATE MAILED: 09/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/019,388

Applicant(s)

GRAVALOS ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-11 and 15 is/are allowed.
- 6) ☒ Claim(s) 12,13,17 and 18 is/are rejected.
- 7) ☒ Claim(s) 14 and 16 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an application filed on 4/23/02. There are eighteen claims pending and eighteen under consideration. Claims 1-11 and 16 are compound claims. Claim 15 is a composition claim. Claim 18 is a use claim. Claims 12-14 and 17 are method of making claims. This is the first action on the merits. The application concerns some 5-hydroxylated derivatives of staurosporine, compositions, and uses thereof.

Claim Objections

2. Objection is made to claim 16 under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The phrase “for use as a medicament” is a statement of intent. This is a purely mental act with no physical consequences. Thus, claim 16 is a compound claim with the same limitations as claim 1.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 provides for the use of the compounds of formula (I), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to convey

reasonably to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants have disclosed one species of microorganism suitable for their process. Their claim potentially covers all microorganisms, which number in the millions. According to the MPEP §II A 2. (a) (ii) "For each claim drawn to a genus: The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus".

5. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using strain CLOCK-002 to prepare

their compounds, does not reasonably provide enablement for employing every unknown microorganism, capable of producing their compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. “The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular microorganism would produce the claimed compounds would require raising the microorganism in culture and screening the fermentation broth for the compounds, a moderate degree of experimentation. b) The direction concerning the additional microorganisms is found in lines 5-14, page 3. This expresses the desire of finding such additional strains. c) There is only a single working example of such a microorganism. d) The nature of the invention is process fermentation, which involves biochemical reactions. e) The state of the art is directions to the microbiologist to go look for a suitable second organism hardly constituted directions to the chemist who would

actually use such a second organism to prepare the claimed compounds. f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Biochemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. h) The breadth of the claims includes all of the hundreds of compounds of formula I as well as the presently unknown list of microorganisms embraced by claim 12.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

6. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating leukemia, lung carcinoma, colon carcinoma, and melanoma, does not reasonably provide enablement for treating all malignant tumors. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with

these claims. Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

To make clearer the lack of enablement for treatment of all cancer, extrinsic evidence is supplied by Draetta (Ann. Reports Med. Chem.), final sentence on page 246 “[a]lthough many still think about the need for a magic bullet as a cure for all cancers, our knowledge of the molecular mechanism underlying this disease make the prospect of developing such a universal cure very unlikely.” Since no universal cure for cancer has been developed, it follows that there is no correlation between the assays relied upon by applicants and the ability to treat all cancers. Thus, those assays are not sufficient to enable such claims.

The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the “tumor” category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

The factors to be considered in making an enablement rejection have been summarized above. a) Determining if any particular cancer would be treatable with Applicants' compounds would require clinical trials in each disease with each compound. Considering the hundreds of compounds covered by formula I and the multitude of different cancers, this is a very large degree of experimentation. b) The direction concerning cancer treatment is found in Applicants' *in vitro* assay described in the paragraph 1 page 4 and paragraph 4, page 12. Applicants disclose no data on the compounds of claim 1. Applicants describe formulations in paragraph 5, page 4, doses in the sixth paragraph of the same page, but no dosing schedules required to practice their invention. c) There is no working example of cancer treatment in man or animal in the specification. d) The claims rejected are drawn to clinical medicine and are therefore physiological in nature. e) The state of the art in cancer therapy is summarized above. f) The artisan using Applicants invention would be a Board Certified physician in oncology with an MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds

of formula I as well as the presently unknown list of diseases embraced by claim 6. Thus, the scope of the claims is broad.

That conclusion that extensive experimentation will be required is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

7. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating leukemia, lung carcinoma, colon carcinoma, and melanoma, does not reasonably provide enablement for preventing any tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the K-252 compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of tumors generally.

Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent tumors generally. That is, the skill is so low that no compound effective generally against tumors generally has ever been found let alone one that can prevent such conditions.

The Examiner suggests deletion of the word “prophylaxis”.

Allowable Subject Matter

8. Claims 1-11 and 15 are allowed. Claim 14 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

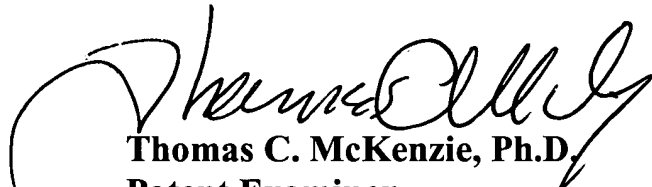
Conclusion

9. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts

Application/Control Number: 10/019,388
Art Unit: 1624

Page 11

to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.


Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK

